# **EAST Search History**

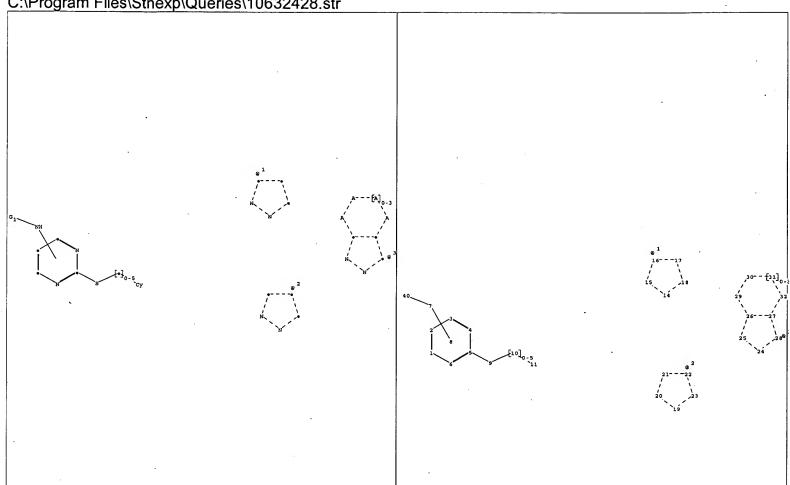
Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	4580	((544/122,295,317) or (514/231.8, 235.8,252.14,274)).CCLS.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2006/10/25 15:17

10/25/2006 3:17:25 PM Page 1

	NPL Search Notes	Results		
13.	TITLE-ABSTR-KEY(inhibiting or inhibition) and TITLE-ABSTR-KEY(catenin) [All Sources(- All Sciences -)]			
12.	TITLE-ABSTR-KEY(inhibiting or inhibition) and TITLE-ABSTR-KEY(tau protein) [All Sources(- All Sciences -)]	295		
11.	TITLE-ABSTR-KEY(lowering) and TITLE-ABSTR-KEY(blood glucose levels) [All Sources(- All Sciences -)]			
10.	TITLE-ABSTR-KEY(glycogen synthesis) and TITLE-ABSTR-KEY(enhancing) [All Sources(- All Sciences -)]			
9.	TITLE-ABSTR-KEY(gsk-3) and TITLE-ABSTR-KEY(hypertrophy) [All Sources(- All Sciences -)]	10		
8.	TITLE-ABSTR-KEY(gsk-3) and TITLE-ABSTR-KEY(cardiomycete hypertrophy) [All Sources(- All Sciences -)]	. 0		
7.	TITLE-ABSTR-KEY(gsk-3) and TITLE-ABSTR-KEY(multiple sclerosis) [All Sources(- All Sciences -)]	0		
6.	TITLE-ABSTR-KEY(gsk-3) and TITLE-ABSTR-KEY(amyotrophic lateral sclerosis or als) [All Sources(- All Sciences -)]			
5.	TITLE-ABSTR-KEY(gsk-3) and TITLE-ABSTR-KEY(diabetes) [All Sources(- All Sciences -)]			
4.	(TITLE-ABSTR-KEY(src) and TITLE-ABSTR-KEY(inhibiting or inhibition or inhibitor)) AND (TITLE-ABSTR-KEY(gsk-3) and TITLE-ABSTR-KEY(inhibiting or inhibition or inhibitor)) [All Sources(- All Sciences -)]	7		
3.	TITLE-ABSTR-KEY(src) and TITLE-ABSTR-KEY(inhibiting or inhibition or inhibitor) [All Sources(- All Sciences -)]	6899		
2.	TITLE-ABSTR-KEY(gsk-3) and TITLE-ABSTR-KEY(inhibiting or inhibition or inhibitor) [All Sources(- All Sciences -)]	593		
1.	TITLE-ABSTR-KEY(aurora-2) and TITLE-ABSTR-KEY(inhibiting or inhibition or inhibitor)  [All Sources(- All Sciences -)]	4		

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C:\Program Files\Stnexp\Queries\10632428.str



chain nodes:

7 9 10 11 40

ring nodes:

1 2 3 4 5 6 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32

chain bonds:

5-9 7-40 9-10 10-11

ring bonds:

1-2 1-6 2-3 3-4 4-5 5-6 14-15 14-18 15-16 16-17 17-18 19-20 19-23 20-21 21-22 22-23 24-25 24-28 25-26 26-27 26-29 27-28 27-32 29-30 30-31 31-32

exact/norm bonds:

5-9 7-40 9-10 10-11 14-15 14-18 15-16 16-17 17-18 19-20 19-23 20-21 21-22 22-23 24-25 24-28 25-26 26-27 26-29 27-28 27-32 29-30 30-31 31-32

normalized bonds:

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems:

containing 1: 14: 19: 24:

## G1:[\*1],[\*2],[\*3]

### Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS8:Atom 9:CLASS10:CLASS11:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 40:CLASS

=>

Uploading C:\Program Files\Stnexp\Queries\10632428.str



```
chain nodes :
7 9 10 11 40
ring nodes :
30 31 32
chain bonds :
5-9 7-40 9-10 10-11
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 14-15 14-18 15-16 16-17 17-18 19-20 19-23
20-21 21-22 22-23 24-25 24-28 25-26 26-27 26-29 27-28 27-32 29-30 30-31
31-32
exact/norm bonds :
5-9 7-40 9-10 10-11 14-15 14-18 15-16 16-17 17-18 19-20 19-23 20-21
21-22 22-23 24-25 24-28 25-26 26-27 26-29 27-28 27-32 29-30 30-31 31-32
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 : 14 : 19 : 24 :
```

#### G1:[\*1],[\*2],[\*3]

#### Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:Atom 9:CLASS 10:CLASS 11:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 40:CLASS

L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

L1 STR

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

Structure attributes must be viewed using STN Express query preparation.

=> s 11 sss sam

SAMPLE SEARCH INITIATED 09:18:37 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 85 TO ITERATE

100.0% PROCESSED 85 ITERATIONS

10 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS:

1147 TO 2253

PROJECTED ANSWERS:

11 TO 389

L2 10 SEA SSS SAM L1

=> => s l1 sss ful

FULL SEARCH INITIATED 09:19:29 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 1696 TO ITERATE

100.0% PROCESSED 1696 ITERATIONS

179 ANSWERS

SEARCH TIME: 00.00.01

L3 179 SEA SSS FUL L1

=> => s 13

L4. 13 L3

=> d 14 1-13 bib, ab, hitstr

- ANSWER 1 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN L4
- 2006:758896 CAPLUS AN
- DN 145:241171
- The Aurora Kinase Inhibitor VX-680 Induces Endoreduplication and Apoptosis ΤI Preferentially in Cells with Compromised p53-Dependent Postmitotic Checkpoint Function
- Gizatullin, Farid; Yao, Xao; Kung, Victor; Harding, Matthew W.; Loda, Massimo; Shapiro, Geoffrey I.

  Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, ΑU
- CS 02115, USA
- Cancer Research (2006), 6(15), 7668-7677SO CODEN: CNREA8; [ISSN: 0008-5472]
- PB American Association for Cancer Research
- DT
- LΑ English
- VX-680 is a potent inhibitor of Aurora kinases that induces the AΒ accumulation of cells with  $\geq 4N$  DNA content, followed by cell death. Here, we define the role of p53 and p21Waf1/Cip1 in cell cycle perturbations following exposure to VX-680. Endoreduplication and apoptosis in response to VX-680 are limited in A549 and MCF-7 cells expressing wild-type p53, and markedly enhanced in cells lacking p53, including those engineered to express the HPV16-E6 oncoprotein or short interfering RNA pools targeting p53. In contrast, endoreduplication and apoptosis occur in the p53 wild-type cell lines, RKO and U2OS. The difference in response to VX-680 among these cell lines correlates with the timing of induction of p21Waf1/Cip1 and its ability to inhibit cyclin E-cdk2 activity. In A549 cells, VX-680 induces the expression of p53 and p21Waf1/Cip1 within 24 h, with consequent inhibition of cyclin E-cdk2, and reduction of retinoblastoma protein phosphorylation, limiting endoreduplication. In RKO and U2OS cells, the induction of p21Waf1/Cip1 is delayed and associated with higher residual cyclin E-cdk2 kinase activity and retinoblastoma protein phosphorylation, followed by progressive endoreduplication and apoptosis. Abrogation of p21Waf1/Cip1 expression by short interfering RNA targeting in A549 cells results in a substantial increase in the degree of endoreduplication, whereas inducible expression of p21Waf1/Cip1 in p53-neg. NCI-H1299 cells inhibits VX-680-induced endoreduplication and cell death. These data suggest that the integrity of the p53-p21Waf1/Cip1-dependent postmitotic checkpoint governs the response to Aurora kinase inhibition. Although cells with intact checkpoint function arrest with 4N DNA content, those with compromised checkpoint function are more likely to undergo endoreduplication followed by eventual apoptosis.
- IT 639089-54-6, VX-680
  - RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (aurora kinase inhibitor VX-680 induces endoreduplication and apoptosis preferentially in cells with compromised p53-dependent postmitotic checkpoint function)
- RN 639089-54-6 CAPLUS
- Cyclopropanecarboxamide, N-[4-[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-CN pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 2 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
L4
AN
          2006:681435 CAPLUS
DN
          145:137879
TI
          Pyrimidine derivative kinase modulators and therapeutic use
          Chen, Jeff; Dalrymple, Lisa Esther; Epshteyn, Sergey; Forsyth, Timothy
IN
          Patrick; Huynh, Tai Phat; Ibrahim, Mohamed Abdulkader; Leahy, James W.;
          Lewis, Gary Lee; Mann, Grace; Mann, Lary W.; Noguchi, Robin Tammie;
          Ridgway, Brian Hugh; Sangalang, Joan Cruz; Schnepp, Kevin Luke; Shi, Xian;
          Takeuchi, Craig Stacy; Williams, Matthew Alan; Nuss, John; Cheung, Atwood
PA
          Exelixis, Inc., USA
SO
          PCT Int. Appl., 194 pp.
          CODEN: PIXXD2
DT
          Patent
LΑ
          English
FAN.CNT 1
          PATENT NO.
                                                  KIND
                                                                                        APPLICATION NO.
                                                                                                                                       DATE
                                                  ____
PΙ
         WO 2006074057 ·
                                                    A2
                                                               20060713
                                                                                        WO 2005-US47402
                                                                                                                                       20051228
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                          VN, YU, ZA, ZM, ZW
                  RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
                         IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
                          GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
                          KG, KZ, MD, RU, TJ, TM
PRAI US 2004-640439P
                                                    Ρ
                                                                20041230
          US 2005-704863P
                                                    Ρ
                                                                20050801
OS
          MARPAT 145:137879
AΒ
          The invention provides pyrimidine derivs. and methods for inhibition of
          kinases, more specifically IGF1R kinases. The invention also provides
          compds. and methods for inhibition of wildtype Abl. The invention
          provides compds. for modulating protein kinase enzymic activity for
          modulating cellular activities such as proliferation, differentiation,
          programmed cell death, migration and chemoinvasion. Compds. of the
          invention inhibit, regulate and/or modulate kinase receptor signal
          transduction pathways related to the changes in cellular activities as
          mentioned above, and the invention includes compns. which contain these
          compds., and methods of using them to treat kinase-dependent diseases and
                                    Preparation of pyrimidine derivs. is included.
          conditions.
          898278-97-2
IT
          RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
          (Biological study); USES (Uses)
                (pyrimidine derivative kinase modulators and therapeutic use)
RN
          898278-97-2 CAPLUS
          Cyclopropanecarboxamide, N-[4-[4-(4-methyl-1-piperazinyl)-6-[(3-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-methyl-1H-
CN
```

pyrazol-5-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

```
L4
     ANSWER 3 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
AN
     2006:495929 CAPLUS
DN
     145:8181
ΤI
     Preparation of pyrazolylamino pyrimidine derivatives as Aurora A/B kinase
     inhibitors
     Xiao, Xiao-Yi; Patel, Dinesh V.
IN
PΑ
     Miikana Therapeutics, Inc., USA
SO
     PCT Int. Appl., 81 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                          KIND
                                  DATE
                                               APPLICATION NO.
                                                                       DATE
ΡI
     WO 2006055831
                           A2
                                  20060526
                                              WO 2005-US41945
                                                                       20051117
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                                           /BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRAI US 2004-629176P
                           Ρ
                                  20041117
     MARPAT 145:8181
AB
     Title compds. represented by the formula I [wherein ring A =
     (un) substituted pyrazolyl; W = (un) substituted amino; X = carboxyl,
     carbonyl ester or aminoacyl; Y = O, S, SO, SO2 or NR; R = H or
     (un) substituted alkyl; Ar = (un) substituted (hetero) aryl; R2 = H or alkyl;
     R3 = H, (un)substituted alkyl, alkoxy, etc.; and isomers, prodrugs, and
     pharmaceutically acceptable salts thereof] were prepared as Aurora A/B
     kinase inhibitors. For example, II was provided in a multi-step synthesis
     starting from potassium salt of 5-nitroorotic acid. Selected I inhibited
     Aurora B enzyme by 100%, and I were tested for Aurora kinase whole cell
     cytoxicity using human tumor-derived cell lines, HCT116 or MCF7.
     Pharmaceutical formulations were given also. Thus, I and their
     pharmaceutical compns. are useful for the prevention or treatment of
     diseases associated with protein kinases, especially diseases associated with
     (Aurora-2) and Aurora-B (Aurora-1), such as cancer.
     888020-14-2P 888020-15-3P 888020-18-6P
     RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
         (preparation of pyrazolylamino pyrimidine derivs. as Aurora A/B kinase
        inhibitors)
RN
     888020-14-2 CAPLUS
     4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe
CN
     nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, methyl ester (9CI)
```

INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

888020-15-3 CAPLUS

4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe CN nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

888020-18-6 CAPLUS

4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe CN nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

888020-16-4P 888020-19-7P 888020-20-0P

888020-21-1P 888020-22-2P 888020-23-3P

888020-24-4P 888020-27-7P 888020-28-8P

888020-29-9P 888020-30-2P 888020-31-3P

888020-32-4P 888020-33-5P 888020-34-6P

888020-35-7P 888020-36-8P 888020-37-9P

888020-38-0P 888020-39-1P 888020-40-4P 888020-41-5P 888020-42-6P 888020-43-7P

888020-44-8P 888020-45-9P 888020-46-0P

888020-47-1P 888020-48-2P 888020-49-3P

888020-50-6P 888020-51-7P 888020-52-8P

888020-53-9P 888020-54-0P 888020-55-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrazolylamino pyrimidine derivs. as Aurora A/B kinase inhibitors)

RN 888020-16-4 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-N-methyl-6-[(5-methyl-1H-pyrazol-3-yl)amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-19-7 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-N-[2-(dimethylamino)ethyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{NH}-\text{C} \\ \text{H}_2\text{N} \\ \text{N} \\ \text{$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-20-0 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe
 nyl]sulfonyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, ethyl ester (9CI) (CA
 INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

RN 888020-21-1 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe nyl]sulfinyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & & & \\ \hline & C-OEt \\ \hline & H_2N & & \\ \hline & N & \\ \hline & N & \\ \hline & N & \\ \hline & NH-C \\ \hline \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-22-2 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-N-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)

RN 888020-23-3 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, 2-(4-morpholinyl)ethyl ester (9CI) (CA INDEX NAME)

$$C = 0$$

NH

N

N

N

N

N

N

C-0-CH<sub>2</sub>-CH<sub>2</sub>-N

Me

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-24-4 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, tetrahydro-2H-pyran-4-yl ester (9CI) (CA INDEX NAME)

RN 888020-27-7 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O \\ \parallel \\ C-O-CH_2-CH_2-OMe \\ \parallel \\ N \\ N \\ \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-28-8 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, 2-(methylthio)ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-29-9 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe

nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, cyclohexyl ester (9CI)
(CA INDEX NAME)

$$\begin{array}{c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-30-2 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-N-(2-methoxyethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-31-3 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[5-amino-4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-morpholinylcarbonyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 888020-32-4 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[5-amino-4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-thiomorpholinylcarbonyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-33-5 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, 2-(dimethylamino)ethyl ester (9CI) (CA INDEX NAME)

RN 888020-34-6 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, 1-methyl-4-piperidinyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-35-7 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, 2-(1-piperidinyl)ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

RN 888020-36-8 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, 1-methylethyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-37-9 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, 2-hydroxyethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

RN 888020-38-0 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-N-4-pyridinyl- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-39-1 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-N-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} C \longrightarrow O \\ NH \\ N \longrightarrow N \longrightarrow N \longrightarrow C \longrightarrow NH_2 \longrightarrow N$$

RN 888020-40-4 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[5-amino-4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(1-piperidinylcarbonyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-41-5 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-N-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)

RN 888020-42-6 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-N-(3-methoxypropyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]- (9CI) (CA INDEX NAME)

HN N N S NH C NH 
$$C$$
 NH  $C$  NH  $C$  NH  $C$  NH  $C$  NH  $C$ 

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-43-7 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-N-[2-(methylthio)ethyl]- (9CI) (CA INDEX NAME)

RN 888020-44-8 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-N-(1,1-dimethylethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-45-9 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-N-(2-furanylmethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} C = O \\ NH \\ NH \\ NH_2 \\ \end{array}$$

RN 888020-46-0 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-N-(2-thienylmethyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c} C = O \\ NH \\ S \\ NH \\ C-NH-CH_2 \\ \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-47-1 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-N-phenyl- (9CI) (CA INDEX NAME)

RN 888020-48-2 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-N-(2-methoxy-1-methylethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & \text{Me} \\ & &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

N 888020-49-3 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-N-cyclohexyl-2-[[4-[(cyclopropylcarbonyl)amino]phenyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} NH \\ C = O \\ NH - C \\ N$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-50-6 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl]

thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-N-(tetrahydro-2H-pyran-4-yl)-(9CI) (CA INDEX NAME)

$$\begin{array}{c} O \\ NH \\ C = O \\ HN \\ N \\ N \\ S \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-51-7 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-N-(1-methyl-4-piperidinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & Me \\ & N \\ & NH \\ & C \\ & O \\ & NH \\ & NH \\ & C \\ & NH \\ & NH \\ & C \\ & Me \\ \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-52-8 CAPLUS

CN 4-Pyrimidinecarboxamide, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phenyl] thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-N-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

RN 888020-53-9 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, phenylmethyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-54-0 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 5-amino-2-[[4-[(cyclopropylcarbonyl)amino]phe nyl]thio]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-, 2-(trimethylsilyl)ethyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-55-1 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[5-amino-4-[(4-methyl-1-piperazinyl)carbonyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

IT 888020-13-1P 888020-17-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyrazolylamino pyrimidine derivs. as Aurora A/B kinase inhibitors)

RN 888020-13-1 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 2-[[4-[(cyclopropylcarbonyl)amino]phenyl]thio ]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-5-nitro-, methyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 888020-17-5 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 2-[[4-[(cyclopropylcarbonyl)amino]phenyl]thio ]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-5-nitro-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

- L4 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
- AN 2006:459089 CAPLUS
- DN 145:43907
- TI Targeting Aurora Kinases for the Treatment of Prostate Cancer
- AU Lee, Edmund Chun Yu; Frolov, Anna; Li, Rile; Ayala, Gustavo; Greenberg, Norman M.
- CS Clinical Research Division, Fred Hutchinson Cancer Research Center, and Department of Pharmacology, University of Washington, Seattle, WA, 98109, USA
- SO Cancer Research ((2006), 66(10), 4996-5002
  - CODEN: CNREA8; issn: 0008-5472
- PB American Association for Cancer Research
- DT Journal
- LA English
- Inappropriate expression of the Aurora kinases can induce aberrant AΒ mitosis, centrosome irregularities, and chromosomal instability, which lead to aneuploidy and cell transformation. Here, we report that Aurora-A and Aurora-B are highly expressed in primary human and mouse prostate cancers and prostate cancer cell lines. In clin. samples, levels of Aurora-A and Aurora-B were significantly elevated in prostatic intraepithelial neoplasia lesions and prostate tumors when compared with the non-neoplastic samples. Interestingly, expression of Aurora-A in non-neoplastic prostates correlated with seminal vesicle invasion ( $\rho$  = 0.275, P = 0.0169) and in prostate tumor with pos. surgical margins (p = 0.265, P = 0.0161). In addition, nuclear expression of Aurora-B in prostatic intraepithelial neoplasia lesions correlated with clin. staging of the tumor ( $\rho = -0.4$ , P = 0.0474) whereas cytoplasmic expression in tumors correlated with seminal vesicle invasion ( $\rho = 0.282$ , P = 0.0098). Cell lines and primary tumors derived from the TRAMP model were also found to express high levels of Aurora-A and Aurora-B. When human PC3, LNCaP, and mouse C1A cells were treated with the potent Aurora kinase inhibitor VX680, which attenuates phosphorylation of histone H3, cancer cell survival was reduced. VX680 could further reduce cell viability >2-fold when used in combination with the chemotherapy drug doxorubicin. Our findings support a functional relationship between Aurora kinase expression and prostate cancer and the application of small-mol. inhibitors in therapeutic modalities.
- IT 639089-54-6, VX680
  - RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (Aurora-A kinase and Aurora-B kinase are highly expressed in primary human and mouse prostate cancers and prostate cancer cell lines and application of small-mol. inhibitors in therapeutic modalities)
- RN 639089-54-6 CAPLUS
- CN Cyclopropanecarboxamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L4 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
- AN 2006:55725 CAPLUS
- DN 144:166361
- TI Structure of the Kinase Domain of an Imatinib-Resistant Abl Mutant in Complex with the Aurora Kinase Inhibitor VX-680
- AU Young, Matthew A.; Shah, Neil P.; Chao, Luke H.; Seeliger, Markus; Milanov, Zdravko V.; Biggs, William H., III; Treiber, Daniel K.; Patel, Hitesh K.; Zarrinkar, Patrick P.; Lockhart, David J.; Sawyers, Charles L.; Kuriyan, John
- CS Departments of Molecular and Cell Biology and Chemistry, Howard Hughes Medical Institute, The University of California, Berkeley, CA, USA
- SO Cancer Research (2006), 66(2), 1007-1014 CODEN: CNREA8; ISSN: 0008-5472
- PB American Association for Cancer Research
- DT Journal
- LA English
- We present a high-resolution (2.0 Å) crystal structure of the catalytic AB domain of a mutant form of the Abl tyrosine kinase (H396P; Abl-la numbering) that is resistant to the Abl inhibitor imatinib. The structure is determined in complex with the small-mol. inhibitor VX-680 (Vertex Pharmaceuticals, Cambridge, MA), which blocks the activity of various imatinib-resistant mutant forms of Abl, including one (T315I) that is resistant to both imatinib and BMS-354825 (dasatinib), a dual Src/Abl inhibitor that seems to be clin. effective against all other imatinib-resistant forms of BCR-Abl. VX-680 is shown to have significant inhibitory activity against BCR-Abl bearing the T315I mutation in patient-derived samples. The Abl kinase domain bound to VX-680 is not phosphorylated on the activation loop in the crystal structure but is nevertheless in an active conformation, previously unobserved for Abl and inconsistent with the binding of imatinib. The adoption of an active conformation is most likely the result of synergy between the His396Pro mutation, which destabilizes the inactive conformation required for imatinib binding, and the binding of VX-680, which favors the active conformation through hydrogen bonding and steric effects. VX-680 is bound to Abl in a mode that accommodates the substitution of isoleucine for threonine at residue 315 (the "gatekeeper" position). The avoidance of the innermost cavity of the Abl kinase domain by VX-680 and the specific recognition of the active conformation explain the effectiveness of this compound against mutant forms of BCR-Abl, including those with mutations at the gatekeeper position.
- IT 639089-54-6D, VX 680, complexes with Abl kinase domain RL: PRP (Properties)
  - (structural and biochem. anal. address mol. basis of VX-680 inhibitory activity against imatinib-resistant mutant forms of human BCR-Abl)
- RN 639089-54-6 CAPLUS
- CN Cyclopropanecarboxamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

- ANSWER 6 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN L4
- AN 2005:781086 CAPLUS
- 143:222029 DN
- TI Inhibition of drug-resistant mutants of ABL, KIT, and EGF receptor kinases
- ΑU Carter, Todd A.; Wodicka, Lisa M.; Shah, Neil P.; Velasco, Anne Marie; Fabian, Miles A.; Treiber, Daniel K.; Milanov, Zdravko V.; Atteridge, Corey E.; Biggs, William H., III; Edeen, Philip T.; Floyd, Mark; Ford, Julia M.; Grotzfeld, Robert M.; Herrgard, Sanna; Insko, Darren E.; Mehta, Shamal A.; Patel, Hitesh K.; Pao, William; Sawyers, Charles L.; Varmus, Harold; Zarrinkar, Patrick P.; Lockhart, David J.
- Ambit, //hc.\ Sah Diego, CA, 92121, USA CS
- Proceedings of the National Academy of Sciences of the United States of SO Americ (2005), 102(31), 11011-11016 CODEN: PNASA6; ISSN: 0027-8424
- National Academy of Sciences PB
- DT Journal
- English LA
- AB To realize the full potential of targeted protein kinase inhibitors for the treatment of cancer, it is important to address the emergence of drug resistance in treated patients. Mutant forms of BCR-ABL, KIT, and the EGF receptor (EGFR) have been found that confer resistance to the drugs imatinib, gefitinib, and erlotinib. The mutations weaken or prevent drug binding, and interestingly, one of the most common sites of mutation in all three kinases is a highly conserved "gatekeeper" threonine residue near the kinase active site. We have identified existing clin. compds. that bind and inhibit drug-resistant mutant variants of ABL, KIT, and We found that the Aurora kinase inhibitor VX-680 and the p38 inhibitor BIRB-796 inhibit the imatinib- and BMS-354825-resistant ABL(T315I) kinase. The KIT/FLT3 inhibitor SU-11248 potently inhibits the imatinib-resistant KIT(V559D/T670I) kinase, consistent with the clin. efficacy of SU-11248 against imatinib-resistant gastrointestinal tumors, and the EGFR inhibitors EKB-569 and Cl-1033, but not GW-572016 and ZD-6474, potently inhibit the gefitinib- and erlotinib-resistant EGFR(L858R/T790M) kinase. EKB-569 and Cl-1033 are already in clin. trials, and our results suggest that they should be considered for testing in the treatment of gefitinib/erlotinib-resistant non-small cell lung cancer. The results highlight the strategy of screening existing clin. compds. against newly identified drug-resistant mutant variants to find compds. that may serve as starting points for the development of next-generation drugs, or that could be used directly to treat patients that have acquired resistance to first-generation targeted therapy. ΙT 639089-54-6, VX-680
  - RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (inhibition of drug-resistant mutants of ABL, KIT, and EGF receptor kinases for screening of antitumor agents)
- RN639089-54-6 CAPLUS
- CN Cyclopropanecarboxamide, N-[4-[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-piperazinyl)-6-[(5-methyl-1pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:140796 CAPLUS

DN 142:240444

TI Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3

IN Bebbington, David; Charrier, Jean-damien; Golec, Julian; Miller, Andrew; Knegtel, Ronald

PA UK

SO U.S. Pat. Appl. Publ., 164 pp. CODEN: USXXCO

DT Patent

LA English

FAN. CNT 1

t MIN.	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
			<del>-</del>		
PI PRAI	US 2005038023 US 2003-632428	A1	20050217 20030801	US 2003-632428	20030801

OS MARPAT 142:240444

AB The title compds. I [Z1 = N, CR8; Z2 = N, CH; and at least one of Z1 and Z2 = N; Rb, Rc = TR3, LZR3; C2RbRc = (un)substituted fused (hetero)cycle; Q = NR4, O, S, etc.; R1 = TD; D = (un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, carbocyclyl; T = a bond, alkylidene (un)interrupted by O, S, NR4, CO, etc.; Z = alkylidene; L = O, S, SO, SO2, etc.; R2, R2a = R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, etc.; R = H, (un)substituted aliphatic, (hetero)aryl, heterocyclyl; R4 = R7, COR7, SO2R7, etc.; W = CO, CO2, CONR6, etc.; R6, R7 = H, alkyl; or N(R6)2 or N(R7)2 = heterocyclyl, heteroaryl] were prepared For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in tert-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20 μM: GSK-3β, AURORA-2, CDK-2, ERK2, AKT, and human Src kinase. I are useful for the treatment of diseases associated with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

IT 438203-38-4P 438203-43-1P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438203-38-4 CAPLUS

CN Acetamide, N-[4-[[4-(4-methoxyphenyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438203-43-1 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-[[4-[(1-oxopropyl)amino]phenyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

IT 438203-35-1P 438203-36-2P 438203-41-9P

438203-45-3P 438203-48-6P 438205-29-9P

438205-30-2P 438205-31-3P 438205-32-4P

438205-34-6P 438205-36-8P 438205-38-0P

438205-40-4P 438205-41-5P 438205-42-6P

438205-43-7P 438205-44-8P 438205-46-0P

438205-47-1P 438205-48-2P 438205-49-3P

438205-50-6P 438205-51-7P 438205-52-8P

438205-53-9P 438205-54-0P 438205-55-1P

438205-56-2P 438205-57-3P 438205-58-4P

438205-59-5P 438205-60-8P 438205-61-9P

438205-62-0P 438205-63-1P 438205-64-2P

438205-65-3P 438205-66-4P 438205-67-5P

438205-68-6P 438205-69-7P 438205-70-0P

438205-71-1P 438205-72-2P 438205-73-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438203-35-1 CAPLUS

CN Acetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 438203-36-2 CAPLUS

CN 4-Pyrimidinamine, 2-[[(4-methoxyphenyl)methyl]thio]-6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-41-9 CAPLUS

CN Acetamide, N-[4-[[4-[4-[3-(dimethylamino)propoxy]phenyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-45-3 CAPLUS

CN Propanamide, N-[4-[[4-(hydroxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

HO-CH<sub>2</sub>

$$NH-C-Et$$

$$NH-C-Et$$
Me

RN 438203-48-6 CAPLUS

CN Acetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-morpholinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-29-9 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-6-phenyl- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-30-2 CAPLUS

CN Benzoic acid, 3-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

RN 438205-31-3 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-(9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-32-4 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-5,6-dimethyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-34-6 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-5-methyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-36-8 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-methyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

RN 438205-38-0 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-40-4 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-(4-methyl-1-piperazinyl)-2-(2-naphthalenylthio)- (9CI) (CA'INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-41-5 CAPLUS

CN 4-Pyrimidinamine, 6-(2,6-dimethylphenyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

438205-42-6 CAPLUS

CN 4-Pyrimidinamine, 6-(2-methylphenyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-(2-methylphenyl)naphthalenylthio) - (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

438205-43-7 CAPLUS RN

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-6phenyl- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN

438205-44-8 CAPLUS Propanamide, 2-methyl-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-CN 2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 4.38205-46-0 CAPLUS

CN Propanamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-47-1 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-48-2 CAPLUS

CN 1-Propanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-49-3 CAPLUS

CN Ethanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-50-6 CAPLUS

CN Acetamide, N-[4-[[4-(2-methylphenyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-51-7 CAPLUS

CN Butanamide, 3-methyl-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

RN 438205-52-8 CAPLUS

CN Acetamide, N-[4-[[5-methyl-4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-53-9 CAPLUS

CN Acetamide, N-[4-[[4-[3-(acetylamino)phenyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-54-0 CAPLUS

CN 2-Propanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-55-1 CAPLUS

CN Acetamide, 2-(dimethylamino)-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-56-2 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-57-3 CAPLUS

CN 4,6-Pyrimidinediamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(2-methoxyethyl)-N'-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

MeO-
$$CH_2$$
- $CH_2$ - $N$ 

N
S- $CH_2$ 

C1

RN 438205-58-4 CAPLUS

CN 4-Pyrimidinamine, 6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-[(phenylmethyl)thio]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-59-5 CAPLUS

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-[(phenylmethyl)thio]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-60-8 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

RN 438205-61-9 CAPLUS

CN Acetamide, N-[4-[[4-(1,1-dimethylethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-62-0 CAPLUS

CN Propanamide, N-[4-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-63-1 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(1-piperidinyl)- (9CI) (CA INDEX NAME)

RN 438205-64-2 CAPLUS

CN Morpholine, 4-[[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-morpholinyl)-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN . 438205-65-3 CAPLUS

CN Morpholine, 4-[[4-[[[4-[(2-methoxyethyl)amino]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 438205-66-4 CAPLUS

CN Morpholine, 4-[[4-[[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-67-5 CAPLUS

CN Propanamide, N-[4-[[4-(methoxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-68-6 CAPLUS

CN Benzoic acid, 4-[[4-(methoxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-69-7 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3,5-dimethoxyphenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-70-0 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3,5-dimethoxyphenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(3-pyrrolidinyl)- (9CI) (CA INDEX NAME)

RN 438205-71-1 CAPLUS

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-[(2-naphthalenylmethyl)thio]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-72-2 CAPLUS

CN Acetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-73-3 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-[[4-[(1-oxopropyl)amino]phenyl]thio]-, butyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:161480 CAPLUS

DN 140:399485

TI VX-680, a potent and selective small-molecule inhibitor of the Aurora kinases, suppresses tumor growth in vivo

AU Harrington, Elizabeth A.; Bebbington, David; Moore, Jeff; Rasmussen, Richele K.; Ajose-Adeogun, Abi O.; Nakayama, Tomoko; Graham, Joanne A.; Demur, Cecile; Hercend, Thierry; Diu-Hercend, Anita; Su, Michael; Golec, Julian M. C.; Miller, Karen M.

CS Vertex Pharmaceuticals (Europe) Limited, Abington, Oxfordshire, OX14 4RY,

SO Nature Medicine (New York, NY, United States) (2004), 10(3), 262-267 CODEN: NAMEFI; ISSN: 1078-8956

PB. Nature Publishing Group

DT Journal

LA English

AB The Aurora kinases are essential for the regulation of chromosome segregation and cytokinesis during mitosis. Aberrant expression and activity of these kinases occur in a wide range of human tumors, and lead to aneuploidy and tumorigenesis. Here we report the discovery of a highly potent and selective small-mol. inhibitor of Aurora kinases, VX-680, that blocks cell-cycle progression and induces apoptosis in a diverse range of human tumor types. This compound causes profound inhibition of tumor growth in a variety of in vivo xenograft models, leading to regression of leukemia, colon and pancreatic tumors at well-tolerated doses. Our data indicate that Aurora kinase inhibition provides a new approach for the treatment of multiple human malignancies.

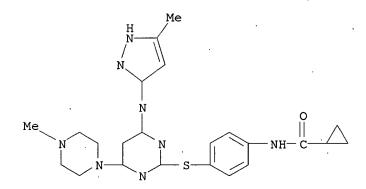
IT 639089-54-6, VX 680

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(VX-680, a potent and selective small-mol. inhibitor of Aurora kinases, suppresses tumor growth in vivo)

RN 639089-54-6 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 9 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
L4
AN
     2004:2878 CAPLUS
     140:59657
DN
     Processes for preparing 6-pyrazolylpyrimidines as inhibitors of protein
TI
     kinase, in particular Aurora kinases, by nucleophilic substitution
     Charrier, Jean-Damien; Mazzei, Francesca; Kay, David; Miller, Andrew
ΙN
                                                              Common you
     Vertex Pharmaceuticals Incorporated, USA
PA
     PCT Int. Appl., 96 pp.
SO
     CODEN: PIXXD2
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     Patent
     English
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     PATENT NO.
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                                 DATE
                                            APPLICATION NO.
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                                            WO 2003-US19266
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    WO 2004000833
                          A1
                                20031231
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
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     JP 2004-515904
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     WO 2003-US19266
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     MARPAT 140:59657
OS
     The present invention provides a facile process for the preparation of tri-and
AB
     tetra-substituted pyrimidines, as inhibitors of protein kinases, especially
     Aurora kinases, by nucleophilic substitution of pyrimidines containing a
     leaving group with a nucleophile in an organic solvent, and optionally in the
     presence of a base. Pyrimidines of the invention are of the formula I
     [wherein Q, T = independently O, S, NR; R = independently H,
     (un) substituted aliphatic group; optionally NR and a radical adjacent to the
     N = 3-7 membered monocyclic, or 8-10 (un)saturated membered bicyclic, bearing
     0-3 addnl. heteroatoms selected from N, O or S; Rx = UR5; R5 = halo, NO,
     CN, R or Ar; U = independently a valence bond, alkylidene chain, with up
     to two methylene units of U optionally and independently replaced by O, S,
     SO, SO2, NRSO, SONR, NR, CO, CO2, NRCO, NRC(O)O, NRCONR, NRSO2NR, CONR,
     OCONR, CR:NNR, CR:NO; Ar = independently (un) substituted 3-7 membered
     monocyclic or 8-10 (un)saturated membered bicyclic, bearing 0-4 heteroatoms
     independently selected from N, O or S; Ry = N(R1), OR1, SR1; R1 =
     independently R, or (un) substituted 3-7 membered monocyclic or 8-10
     (un)saturated membered bicyclic, bearing 0-4 heteroatoms independently
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selected from N, O or S; Rz1 = (un)substituted aliphatic group or 3-8

membered monocyclic, or 8-10 membered bicyclic, or 10-12 membered (un)saturated tricyclic ring bearing 0-4 heteroatoms independently selected from O, N, or S; Rz2 = (un)substituted aliphatic group or 3-8 membered monocyclic, or (un)saturated 8-10 membered bicyclic bearing 0-4 heteroatoms independently selected from N, o or S]. The advantages include min. number of chemical and separation steps, use of available starting materials and simple

reaction media, an easy to scale-up and cheap process. For example, II was prepared by successive nucleophilic substitutions of 2-methylsulfonyl-4,6-dichloropyrimidine (preparation given) with cyclopropanecarboxylic acid N-(4-sulfanylphenyl)amide in tert-BuOH, with 3-amino-5-methylpyrazole in DMF in the presence of DIPEA/NaI, and with N-methylpiperazine in excess. Selected II were found inhibitors of Aurora-1, Aurora-2, Aurora-3, and FLT-3 kinases in vivo, in vitro and in a cell line assay (no data). Thus, selected II and their pharmaceutical compns. are useful for treating or lessening the severity of Aurora-mediated diseases or conditions such as cancer.

IT 639090-55-4P, Cyclopropanecarboxylic acid N-[4-[[4-chloro-6-(5-methyl-2H-pyrazol-3-ylamino)pyrimidin-2-yl]sulfanyl]phenyl]amide RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; process for preparation of 6-pyrazolylpyrimidines, as inhibitors of protein kinase, by nucleophilic substitution)

RN 639090-55-4 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-chloro-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

IT 639089-55-7P 639089-56-8P 639089-57-9P

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(process for preparation of 6-pyrazolylpyrimidines, as inhibitors of protein kinase, by nucleophilic substitution)

RN 639089-55-7 CAPLUS

CN Propanamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(1-piperazinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639089-56-8 CAPLUS

CN Propanamide, 2,2-dimethyl-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(1-piperazinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H & Me \\ \hline N & \\ N &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-57-9 CAPLUS

CN Propanamide, N-[4-[[4-[4-(1-methylethyl)-1-piperazinyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

1T 639090-56-5, Ethanecarboxylic acid N-[4-[[4-chloro-6-(5-methyl-2H-pyrazol-3-ylamino)pyrimidin-2-yl]sulfanyl]phenyl]amide

RL: RCT (Reactant); RACT (Reactant or reagent) (process for preparation of 6-pyrazolylpyrimidines, as inhibitors of protein kinase, by nucleophilic substitution) 639090-56-5 CAPLUS RN Propanamide, N-[4-[[4-chloro-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-CN pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 639090-38-3P 639090-39-4P 639090-40-7P 639090-42-9P 639090-44-1P 639090-46-3P

639090-48-5P 639090-49-6P 639090-50-9P

639090-51-0P

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

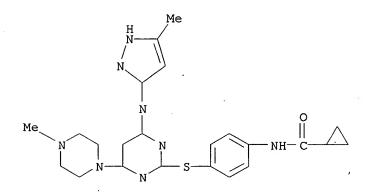
(protein kinase inhibitor, pyrimidine product; process for preparation of 6-pyrazolylpyrimidines, as inhibitors of protein kinase, by nucleophilic substitution)

RN 639090-38-3 CAPLUS

CN Propanedioic acid, compd. with N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1-pipemethyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]cyclopropanecarbox amide (9CI) (CA INDEX NAME)

CM 1

CRN 639089-54-6 CMF C23 H28 N8 O S



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2 CRN 141-82-2 CMF C3 H4 O4

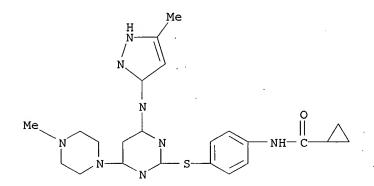
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RN 639090-39-4 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]-, (2E)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 639089-54-6 CMF C23 H28 N8 O S



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

CRN 110-17-8 CMF C4 H4 O4

Double bond geometry as shown.

HO2C E CO2H

RN 639090-40-7 CAPLUS

CN Butanedioic acid, compd. with N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]cyclopropanecarbox amide (9CI) (CA INDEX NAME)

CM 1

CRN 639089-54-6 CMF C23 H28 N8 O S

CM 2

CRN 110-15-6 CMF C4 H6 O4

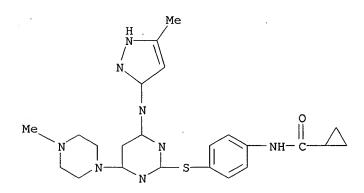
 $HO_2C-CH_2-CH_2-CO_2H$ 

RN 639090-42-9 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 639089-54-6 CMF C23 H28 N8 O S



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

CRN 110-16-7 CMF / C4 H4 O4 Double bond geometry as shown.

RN 639090-44-1 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]-, (2R,3R)-2,3-dihydroxybutanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 639089-54-6 CMF C23 H28 N8 O S

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RN 639090-46-3 CAPLUS

CN Propanoic acid, 3-sulfo-, compd. with N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]cyclopropaneca rboxamide (9CI) (CA INDEX NAME)

CM 1

CRN 639089-54-6

CMF C23 H28 N8 O S

$$\begin{array}{c} H \\ N \\ N \\ N \\ N \\ N \\ N \\ S \\ \end{array} \begin{array}{c} O \\ N \\ N \\ C \\ \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

CRN 44826-45-1 CMF C3 H6 O5 S

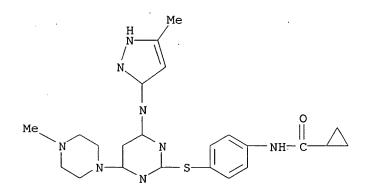
 $HO_2C-CH_2-CH_2-SO_3H$ 

RN 639090-48-5 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]-, 2-hydroxy-1,2,3-propanetricarboxylate (9CI) (CA INDEX NAME)

 $\mathtt{CM} \quad 1$ 

CRN 639089-54-6 CMF C23 H28 N8 O S



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

CRN 77-92-9

CMF C6 H8 O7

$$\begin{array}{c} \text{CO}_2\text{H} \\ | \\ \text{HO}_2\text{C} - \text{CH}_2 - \text{C} - \text{CH}_2 - \text{CO}_2\text{H} \\ | \\ \text{OH} \end{array}$$

RN 639090-49-6 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]-, phosphate (9CI) (CA INDEX NAME)

CM 1

CRN 639089-54-6 CMF C23 H28 N8 O S

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

CRN 7664-38-2 CMF H3 O4 P

RN 639090-50-9 CAPLUS

CN Propanamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]-, hydrochloride (9CI) (CA INDEX NAME)

●x HCl

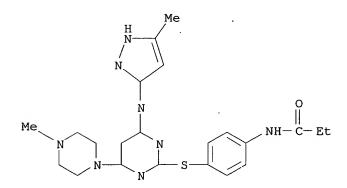
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-51-0 CAPLUS

CN Propanamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 639089-73-9 CMF C22 H28 N8 O S

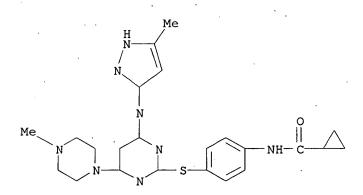


ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

CRN 75-75-2 CMF C H4 O3 S

639089-54-6P, Cyclopropanecarboxylic acid N-[4-[4-(4-IT methylpiperazin-1-yl)-6-(5-methyl-2H-pyrazol-3-ylamino)pyrimidin-2y1]sulfany1]pheny1]amide 639089-58-0P, N-[4-[[4-(5-Methy1-2Hpyrazol-3-ylamino)-6-(4-propylpiperazin-1-yl)pyrimidin-2yl]sulfanyl]phenyl]propionamide 639089-59-1P 639089-60-4P 639089-61-5P 639089-62-6P 639089-63-7P 639089-64-8P 639089-65-9P 639089-66-0P 639089-67-1P 639089-68-2P 639089-69-3P 639089-70-6P 639089-71-7P 639089-72-8P, Cyclopropanecarboxylic acid N-[4-[[4-(4-methyl-4oxopiperazin-1-yl)-6-(5-methyl-2H-pyrazol-3-ylamino)pyrimidin-2yl]sulfanyl]phenyl]amide 639089-73-9P 639090-36-1P 639090-37-2P 639090-58-7P RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (protein kinase inhibitor; process for preparation of 6pyrazolylpyrimidines, as inhibitors of protein kinase, by nucleophilic substitution) RN 639089-54-6 CAPLUS CN Cyclopropanecarboxamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1Hpyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 639089-58-0 CAPLUS

CN Propanamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-propyl-1-piperazinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ N & & & \\ N &$$

RN 639089-59-1 CAPLUS

CN Propanamide, N-[4-[[4-(4-ethyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-60-4 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(1-piperazinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-61-5 CAPLUS

CN Propanamide, N-[4-[[4-[4-(cyclopropylmethyl)-1-piperazinyl]-6-[(5-methyl-

1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-62-6 CAPLUS

CN Propanamide, N-[4-[[4-(4-cyclopropyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-63-7 CAPLUS

CN Propanamide, N-[4-[[4-[4-(1,1-dimethylethyl)-1-piperazinyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639089-64-8 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-ethyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-65-9 CAPLUS

CN Propanamide, N-[4-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-(1-piperazinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639089-66-0 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-ethyl-1-piperazinyl)-6-[(5-ethyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-67-1 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-(4-ethyl-1-piperazinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-68-2 CAPLUS

CN Propanamide, N-[4-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-(4-methyl-1-piperazinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-69-3 CAPLUS

CN Acetamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-70-6 CAPLUS

CN Propanamide, 2,2-dimethyl-N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} H \\ N \\ N \\ N \\ \end{array}$$

RN 639089-71-7 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(5-ethyl-1H-pyrazol-3-yl)amino]-6-(4-methyl-1-piperazinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-72-8 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-methyl-4-oxido-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 639089-73-9 CAPLUS

CN Propanamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-36-1 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]-, hydrochloride (9CI) (CA INDEX NAME)

•x HCl

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-37-2 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 639089-54-6 CMF C23 H28 N8 O S

CM 2

CRN 75-75-2 CMF C H4 O3 S

RN 639090-58-7 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]-, sulfate (9CI) (CA INDEX NAME)

CM 1

CRN 639089-54-6 CMF C23 H28 N8 O S

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

CM 2

CRN 7664-93-9 CMF H2 O4 S

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IT
     639089-74-0P 639089-75-1P 639089-76-2P
     639089-77-3P 639089-78-4P 639089-79-5P
     639089-80-8P 639089-81-9P 639089-82-0P
     639089-83-1P 639089-84-2P 639089-85-3P
     639089-86-4P 639089-87-5P 639089-88-6P
     639089-89-7P 639089-90-0P 639089-91-1P
     639089-92-2P 639089-93-3P 639089-94-4P
     639089-95-5P 639089-96-6P 639089-98-8P
     639090-00-9P 639090-01-0P 639090-02-1P
     639090-03-2P 639090-04-3P 639090-05-4P
     639090-06-5P 639090-07-6P 639090-08-7P
     639090-09-8P 639090-10-1P 639090-11-2P
     639090-12-3P 639090-13-4P 639090-14-5P
     639090-15-6P 639090-16-7P 639090-17-8P
     639090-18-9P 639090-19-0P 639090-20-3P
     639090-21-4P 639090-22-5P 639090-23-6P
     639090-24-7P 639090-25-8P 639090-26-9P
     639090-27-0P 639090-30-5P 639090-35-0P
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
     (Preparation)
        (substituted pyrimidine product; process for preparation of
        6-pyrazolylpyrimidines, as inhibitors of protein kinase, by
       nucleophilic substitution)
RN
     639089-74-0 CAPLUS
CN
     Propanamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-morpholinyl)-
     2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)
```

RN

639089-75-1 CAPLUS
Propanamide, N-[4-[[4-[(2-aminoethyl)amino]-6-[(5-methyl-1H-pyrazol-3-CNyl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

639089-76-2. CAPLUS

CN Propanamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-[[2-(1-yl)piperidinyl)ethyl]amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

639089-77-3 CAPLUS RN

CNmorpholinyl)ethyl]-1-piperazinyl]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639089-78-4 CAPLUS

CN Propanamide, N-[4-[[4-[methyl[2-(methylamino)ethyl]amino]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{Me} & \\ & \text{N-CH}_2\text{-CH}_2\text{-NHMe} & \text{O} \\ & \text{NH-C-Et} \\ & \text{NH-C-Et} \\ & \text{Me} \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-79-5 CAPLUS

CN Propanamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(1-piperidinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

639089-80-8 CAPLUS RN

Propanamide, N-[4-[[4-(hexahydro-1H-1,4-diazepin-1-yl)-6-[(5-methyl-1H-CN pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN

639089-81-9 CAPLUS Propanamide, N-[4-[[4-[[2-(dimethylamino)ethyl]amino]-6-[(5-methyl-1H-1)]CN pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{N} \\ \text{N} \\$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

639089-82-0 CAPLUS RN

Propanamide, N-[4-[[4-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)-6-[(5-CN methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639089-83-1 CAPLUS

CN Propanamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-thiomorpholinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-84-2 CAPLUS

CN Propanamide, N-[4-[[4-[4-(2-hydroxyethyl)-1-piperazinyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639089-85-3 CAPLUS

CN Carbamic acid, [1-[6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-[[4-[(1-oxopropyl)amino]phenyl]thio]-4-pyrimidinyl]-4-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-86-4 CAPLUS

CN Propanamide, N-[4-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-[4-(phenylmethyl)-1-piperazinyl]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639089-87-5 CAPLUS

CN Propanamide, N-[4-[[4-(4-amino-1-piperidinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-88-6 CAPLUS

CN Propanamide, N-[4-[[4-(3-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639089-89-7 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[6-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-2-[[4-[(1-oxopropyl)amino]phenyl]thio]-4-pyrimidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-90-0 CAPLUS

CN Propanamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-phenyl-1-piperazinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639089-91-1 CAPLUS

CN Propanamide, N-[4-[[4-(3,5-dimethyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-92-2 CAPLUS

CN Propanamide, N-[4-[[4-(3-amino-1-pyrrolidinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN

639089-93-3 CAPLUS
Propanamide, N-[4-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-(4-methyl-1-CNpiperidinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-94-4 CAPLUS

Cyclopropanecarboxamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-[[2-CN (1-piperidinyl)ethyl]amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\$$

RN 639089-95-5 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-[[2-(4-morpholinyl)ethyl]amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639089-96-6 CAPLUS

CN Propanamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-piperidinylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639089-98-8 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} H \\ N \\ N \\ N \\ N \\ N \\ N \\ S \\ \end{array} \begin{array}{c} O \\ N \\ N \\ C \\ \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-00-9 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-morpholinyl)-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639090-01-0 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[4-(2-hydroxyethyl)-1-piperazinyl]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-02-1 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[4-(1-methylethyl)-1-piperazinyl]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639090-03-2 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-[[2-(1-pyrrolidinyl)ethyl]amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-04-3 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[[2-(1-piperidinyl)ethyl]amino]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-05-4 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639090-06-5 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(1-piperazinyl)-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H \\ N \\ N \\ N \\ N \\ N \\ S \\ \end{array} \begin{array}{c|c} O \\ 0 \\ 0 \\ 0 \\ \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-07-6 CAPLUS

CN Propanamide, N-[4-[[4-(4-methyl-1-piperazinyl)-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639090-08-7 CAPLUS

CN Propanamide, N-[4-[[4-(4-morpholinyl)-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-09-8 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[[2-(dimethylamino)ethyl]amino]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-10-1 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[[2-(4-morpholinyl)ethyl]amino]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639090-11-2 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[4-(2-cyanoethyl)-1-piperazinyl]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-12-3 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(1H-pyrazol-3-ylamino)-6-[[2-(1-pyrrolidinyl)ethyl]amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639090-13-4 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(2R)-bicyclo[2.2.2]oct-2-ylamino]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-14-5 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(2S)-bicyclo[2.2.2]oct-2-ylamino]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 639090-15-6 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(3,4-dihydro-2(1H)-isoquinolinyl)-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-16-7 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[4-(methylsulfonyl)-1-piperazinyl]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\$$

RN 639090-17-8 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-ethyl-1-piperazinyl)-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-18-9 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(4-propyl-1-piperazinyl)-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-19-0 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[4-[2-(methylsulfonyl)ethyl]-1-piperazinyl]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639090-20-3 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(3-methyl-1-piperazinyl)-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} H \\ N \\ S \\ \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-21-4 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[4-[4-[4-(4-morpholinyl)-2-oxoethyl]-1-piperazinyl]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$C = O$$

NH

S

N

N

N

N

N

CH2

CH2

CH2

RN 639090-22-5 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[4-(phenylmethyl)-1-piperazinyl]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & H & \\ & N &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-23-6 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-[4-(phenylmethyl)-1-piperazinyl]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 639090-24-7 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(3R,5S)-3,5-dimethyl-1-piperazinyl]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-25-8 CAPLUS

CN Propanamide, N-[4-[[4-(methylphenylamino)-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-26-9 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-(diethylamino)-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-27-0 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[4-(1,1-dimethylethyl)-1-piperazinyl]-6-(1H-pyrazol-3-ylamino)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-30-5 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(5-chloro-1H-pyrazol-3-yl)amino]-6-(4-methyl-1-piperazinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} H \\ N \\ N \\ N \\ N \\ N \\ N \\ S \\ \end{array} \begin{array}{c} O \\ N \\ N \\ C \\ \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 639090-35-0 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-morpholinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 10 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
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     2002:615605 CAPLUS
     137:169539
DN
     Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase
ΤI
     inhibitors, especially of Aurora-2 and GSK-3, for treatment of cancer,
     diabetes, and Alzheimer's disease
     Bebbington, David; Charrier, Jean-Damien; Golec, Julian M. C.; Miller,
IN
                                                                 Common Jun.
     Andrew; Knegtel, Ronald
     Vertex Pharmaceuticals Incorporated, USA
PA
SO
     PCT Int. Appl., 335 pp.
     CODEN: PIXXD2
DT
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                                20011220
OS
     MARPAT 137:169539
AB
     285 Title compds. I [wherein Z1 = N or CR8; Z2 = N or CH; and at least 1
     of Z1 and Z2 = N; Rx and Ry = independently TR3 or LZR3; or C2RxRy =
     (un) substituted fused (hetero) cycle; Q = NR4, O, S, C(R6')2,
     1,2-cyclo(prop/but)anediyl, or 1,3-cyclobutanediyl; R1 = TD; D =
     (un) substituted mono- or bicyclic (hetero) aryl, heterocyclyl, or
     carbocyclyl; T = a bond or alkylidene chain (un)interrupted by O, S, NR4,
     CO, CONH, NHCO, SO2, SO2NH, NHSO2, CO2, OCO, OCONH, or NHCO2, with
     provisos; Z = alkylidene chain; L = O, S, SO, SO2, NR6SO2, SO2NR6, NR6,
     NR6CO, NR6CO2, NR6CONR6, NR6SO2NR6, NR6NR6, OCONR6, or W; R2 and R2a =
     independently R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle;
     R3 = R, halo, OR, COR, CO2R, CO(CH2)0-1COR, NO2, CN, SO0-2R, N(R4)2,
     carbamoyl, sulfamoyl, OCOR, acylamino, hydrazino, ureido, etc.; R =
     independently H or (un) substituted aliphatic, (hetero) aryl, or heterocyclyl;
     R4 = independently R7, COR7, carboxy, CON(R7)2, or SO2R7; W = CO, CO2,
     CONR6, C(R6)20, C(R6)2SO0-2, C(R6)2SO2NR6, C(R6)2NR6, C(R6)2NR6CO,
     C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, or
     C(R6) 2NR6CONR6; R6, R6', R7 = independently H or aliphatic; or N(R6) 2 or
     N(R7)2 = independently heterocyclyl or heteroaryl; or C(R6')2 =
     carbocycle; R8 = R, halo, OR, COR, CO2R, COCOR, NO2, CN, SO0-2R, N(R4)2,
     CON(R4)2, SO2(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2,
     C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2] were prepared
     However, the claims pertain only to 3-(2-amino-4-pyrimidinylamino)-1H-
     pyrazoles, i.e. Z1 = Z2 = N, and Q = NH. I are protein kinase inhibitors,
     especially of Aurora-2 and GSK-3. For example, the (pyrazolylamino)quinazoline
     II was refluxed with thiophenol in t-BuOH to give III. In bioassays, I
     inhibited the following kinases with Ki values reported < 20 μM:
     GSK-3\beta (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.),
     ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.).
     are useful for the treatment of diseases associated with protein kinases,
     such as diabetes, cancer, and Alzheimer's disease (no data).
IT
     438203-38-4P, [2-(4-Acetamidophenylsulfanyl)-6-(4-
     methoxyphenyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine
     438203-43-1P, [6-Methoxycarbonyl-2-(4-
     propionylaminophenylsulfanyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-
     yl)amine
```

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438203-38-4 CAPLUS

CN Acetamide, N-[4-[[4-(4-methoxyphenyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-43-1 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-[[4-[(1-oxopropyl)amino]phenyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

438203-35-1P, [2-(4-Acetamidophenylsulfanyl)-6-phenylpyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine 438203-36-2P,

[2-(4-Methoxybenzylsulfanyl)-6-(4-methylpiperazin-1-yl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine 438203-41-9P, [2-(4-Acetamidophenylsulfanyl)-6-[4-(3-dimethylaminopropoxy)phenyl]pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine 438203-45-3P,

[6-Hydroxymethyl-2-(4-propionylaminophenylsulfanyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine 438203-48-6P, [2-(4-Acetamidophenylsulfanyl)-6-(morpholin-4-yl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)[2-(naphthalen-2-ylsulfanyl)-6-phenylpyrimidin-4-yl]amine 438205-30-2P, (5-Cyclopropyl-1H-pyrazol-3-yl)[2-(3-methoxycarbonylphenylsulfanyl)-6-phenylpyrimidin-4-yl]amine 438205-31-3P, (5-Cyclopropyl-1H-pyrazol-3-yl)[2-(naphthalen-2-

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ylsulfanyl)pyrimidin-4-yl]amine 438205-32-4P,
(5-Cyclopropyl-1H-pyrazol-3-yl)[5,6-dimethyl-2-(naphthalen-2-
ylsulfanyl)pyrimidin-4-yl]amine 438205-34-6P,
(5-Cyclopropyl-1H-pyrazol-3-yl)[5-methyl-2-(naphthalen-2-
ylsulfanyl)pyrimidin-4-yl]amine 438205-36-8P,
(5-Cyclopropyl-1H-pyrazol-3-yl)[6-methyl-2-(naphthalen-2-
ylsulfanyl)pyrimidin-4-yl]amine 438205-38-0P,
(5-Cyclopropyl-1H-pyrazol-3-yl)[6-(morpholin-4-yl)-2-(naphthalen-2-
ylsulfanyl)pyrimidin-4-yl]amine 438205-40-4P,
(5-Cyclopropyl-1H-pyrazol-3-yl)[6-(1-methylpiperazin-4-yl)-2-(naphthalen-2-
ylsulfanyl)pyrimidin-4-yl]amine 438205-41-5P,
[6-(2,6-Dimethylphenyl)-2-(naphthalen-2-ylsulfanyl)pyrimidin-4-yl](5-
methyl-1H-pyrazol-3-yl)amine 438205-42-6P, [6-(2-Methylphenyl)-2-
(naphthalen-2-ylsulfanyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine
438205-43-7P, (5-Methyl-1H-pyrazol-3-yl)[2-(naphthalen-2-
ylsulfanyl)-6-phenylpyrimidin-4-yl]amine 438205-44-8P,
[2-(4-Isobutyrylylaminophenylsulfanyl)-6-phenylpyrimidin-4-yl](5-methyl-1H-
pyrazol-3-yl)amine 438205-46-0P, (5-Methyl-1H-pyrazol-3-yl)[6-
phenyl-2-(4-propionylaminophenylsulfanyl)pyrimidin-4-yl]amine
438205-47-1P, [2-(4-Cyclopropylcarbonylaminophenylsulfanyl)-6-
phenylpyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine 438205-48-2P
  (5-Methyl-1H-pyrazol-3-yl)[6-phenyl-2-[[4-(propylsulfonylamino)phenyl]su
lfanyl]pyrimidin-4-yl]amine 438205-49-3P, [2-(4-
Ethanesulfonylaminophenylsulfanyl)-6-phenylpyrimidin-4-yl](5-methyl-1H-
pyrazol-3-yl)amine 438205-50-6P, [2-(4-Acetamidophenylsulfanyl)-
6-(2-methylphenyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine
438205-51-7P, [2-(4-Isobutylcarbonylaminophenylsulfanyl)-6-
phenylpyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine 438205-52-8P
, [2-(4-Acetamidophenylsulfanyl)-5-methyl-6-phenylpyrimidin-4-yl](5-methyl-
1H-pyrazol-3-yl)amine 438205-53-9P, [6-(3-Acetamidophenyl)-2-(4-
acetamidophenylsulfanyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine
438205-54-0P, [2-(4-Isopropylsulfonylaminophenylsulfanyl)-6-
phenylpyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine 438205-55-1P
, [2-[[4-(2-Dimethylaminoacetylamino)phenyl]sulfanyl]-6-phenylpyrimidin-4-
yl](5-methyl-1H-pyrazol-3-yl)amine 438205-56-2P
438205-57-3P 438205-58-4P, [2-Benzylsulfanyl-6-(4-
methylpiperazin-1-yl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine
438205-59-5P 438205-60-8P 438205-61-9P,
[2-(4-Acetamidophenylsulfanyl)-6-tert-butylpyrimidin-4-yl](5-methyl-1H-
pyrazol-3-yl) amine 438205-62-0P, (5-Cyclopropyl-1H-pyrazol-3-yl)
yl) [6-phenyl-2-(4-propionylaminophenylsulfanyl)pyrimidin-4-yl]amine
438205-63-1P 438205-64-2P, (5-Methyl-1H-pyrazol-3-yl)[2-
[[4-(morpholinosulfonyl)benzyl]sulfanyl]-6-morpholin-4-ylpyrimidin-4-
yl]amine 438205-65-3P, [6-(2-Methoxyethylamino)-2-[[4-
(morpholinosulfonyl)benzyl]sulfanyl]pyrimidin-4-yl](5-methyl-1H-pyrazol-3-
yl)amine 438205-66-4P, [6-(4-Methylpiperazin-1-yl)-2-[[4-
(morpholinosulfonyl)benzyl]sulfanyl]pyrimidin-4-yl](5-methyl-1H-pyrazol-3-
yl)amine 438205-67-5P, [6-Methoxymethyl-2-(4-
propionylaminophenylsulfanyl)pyrimidin-4-yl]-(5-methyl-1H-pyrazol-3-
yl)amine 438205-68-6P, [2-(4-Methoxycarbonylphenylsulfanyl)-6-
methoxymethylpyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine
438205-69-7P, [2-(3,5-Dimethoxybenzylsulfanyl)-6-morpholin-4-
ylpyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine 438205-70-0P,
[2-(3,5-Dimethoxybenzylsulfanyl)-6-pyrrolidin-4-ylpyrimidin-4-yl] (5-methyl-
1H-pyrazol-3-yl)amine 438205-71-1P, (5-Methyl-1H-pyrazol-3-yl)[6-
morpholin-4-yl-2-(naphthalene-2-ylmethylsulfanyl)pyrimidin-4-yl]amine
438205-72-2P, [2-(4-Acetamidophenylsulfanyl)pyrimidin-4-yl] (5-
methyl-1H-pyrazol-3-yl)amine 438205-73-3P,
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[6-(1-Butoxycarbonyl)-2-(4-propionylaminophenylsulfanyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438203-35-1 CAPLUS

CN Acetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-36-2 CAPLUS

CN 4-Pyrimidinamine, 2-[[(4-methoxyphenyl)methyl]thio]-6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-41-9 CAPLUS

CN Acetamide, N-[4-[4-[4-[3-(dimethylamino)propoxy]phenyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438203-45-3 CAPLUS

CN Propanamide, N-[4-[[4-(hydroxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-48-6 CAPLUS

CN Acetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-morpholinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-29-9 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-6-phenyl-(9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-30-2 CAPLUS

CN Benzoic acid, 3-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-31-3 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-(9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-32-4 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-5,6-dimethyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

RN 438205-34-6 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-5-methyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-36-8 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-methyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

,RN 438205-38-0 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-40-4 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-(4-methyl-1-piperazinyl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

RN 438205-41-5 CAPLUS

CN 4-Pyrimidinamine, 6-(2,6-dimethylphenyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-42-6 CAPLUS

CN 4-Pyrimidinamine, 6-(2-methylphenyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

RN 438205-43-7 CAPLUS

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-6-phenyl-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-44-8 CAPLUS

CN Propanamide, 2-methyl-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-46-0 CAPLUS

CN Propanamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-47-1 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-48-2 CAPLUS

CN 1-Propanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-49-3 CAPLUS

CN Ethanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-50-6 CAPLUS

CN Acetamide, N-[4-[[4-(2-methylphenyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-51-7 CAPLUS

CN Butanamide, 3-methyl-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-52-8 CAPLUS

CN Acetamide, N-[4-[[5-methyl-4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-53-9 CAPLUS

CN Acetamide, N-[4-[[4-[3-(acetylamino)phenyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-54-0 CAPLUS

CN 2-Propanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-55-1 CAPLUS

CN Acetamide, 2-(dimethylamino)-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

RN 438205-56-2 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-57-3 CAPLUS

CN 4,6-Pyrimidinediamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(2-methoxyethyl)-N'-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-58-4 CAPLUS

CN 4-Pyrimidinamine, 6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-[(phenylmethyl)thio]- (9CI) (CA INDEX NAME)

RN 438205-59-5 CAPLUS

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-[(phenylmethyl)thio]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-60-8 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-61-9 CAPLUS

CN Acetamide, N-[4-[[4-(1,1-dimethylethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-62-0 CAPLUS

CN Propanamide, N-[4-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-63-1 CAPLUS

- CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(1-piperidinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-64-2 CAPLUS

CN Morpholine, 4-[[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-morpholinyl)-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 438205-65-3 CAPLUS

CN Morpholine, 4-[[4-[[4-[(2-methoxyethyl)amino]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

MeO-CH<sub>2</sub>-CH<sub>2</sub>-N

N
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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-66-4 CAPLUS

CN Morpholine, 4-[[4-[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 438205-67-5 CAPLUS

CN Propanamide, N-[4-[[4-(methoxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & & & & \\ & & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ & & \\ & \\ & \\ & \\ & & \\ &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-68-6 CAPLUS

CN Benzoic acid, 4-[[4-(methoxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

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RN 438205-69-7 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3,5-dimethoxyphenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-70-0 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3,5-dimethoxyphenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(3-pyrrolidinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-71-1 CAPLUS

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-[(2-naphthalenylmethyl)thio]- (9CI) (CA INDEX NAME)

RN 438205-72-2 CAPLUS

CN Acetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-73-3 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-[[4-[(1-oxopropyl)amino]phenyl]thio]-, butyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & O & O \\ C - OBu - n & O \\ N & N + C - Et \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 11 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
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AN
     2002:575069 CAPLUS
     137:109292
DN
     Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase
TI
     inhibitors, especially of Aurora-2 and GSK-3, for treatment of cancer,
     diabetes, and Alzheimer's disease
     Bebbington, David; Charrier, Jean-Damien; Davies, Robert; Golec, Julian;
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     Kay, David; Knegtel, Ronald; Patel, Sanjay
     Vertex Pharmaceutical's Incorporated, USA
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     PCT Int. Appl., 337 pp.
     CODEN: PIXXD2
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OS MARPAT 137:109292

AB

Title compds. I [wherein Z1 = N or CR8; Z2 = N or CH; and at least 1 of Z1and Z2 = N; Rx and Ry = independently TR3 or LZR3; or C2RxRy = (un) substituted fused (hetero) cycle; Q = NR4, O, S, C(6a)2, 1,2-cyclo(prop/but)anediyl, or 1,3-cyclobutanediyl; R1 = TD; D = (un) substituted mono- or bicyclic (hetero) aryl, heterocyclyl, or carbocyclyl; T = a bond or alkylidene chain (un)interrupted by O, S, NR4, CO, CONH, NHCO, SO2, SO2NH, NHSO2, CO2, OCO, OCONH, or NHCO2, with provisos; Z = alkylidene chain; L = O, S, SO, SO2, NR6SO2, SO2NR6, NR6, NR6CO, NR6CO2, NR6CONR6, NR6SO2NR6, NR6NR6, OCONR6, or W; R2 and R2a = independently R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, COR, CO2R, CO(CH2)0-1COR, NO2, CN, SO0-2R, N(R4)2, carbamoyl, sulfamoyl, OCOR, acylamino, hydrazino, ureido, etc.; R = independently H or (un) substituted aliphatic, (hetero) aryl, or heterocyclyl; R4 = independently R7, COR7, carboxy, CON(R7)2, or SO2R7; W = CO, CO2, CONR6, C(R6)20, C(R6)2SO0-2, C(R6)2SO2NR6, C(R6)2NR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, or C(R6) 2NR6CONR6; R6, R6a, R7 = independently H or aliphatic; or N(R6)2 orN(R7)2 = independently heterocyclyl or heteroaryl; or C(R6a)2 = carbocycle; R8 = R, halo, OR, COR, CO2R, COCOR, NO2; CN, SO0-2R, N(R4)2, CON(R4)2, SO2(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2] were prepared I are protein kinase inhibitors, especially of Aurora-2 and GSK-3. For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in t-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20  $\mu$ M: GSK-3 $\beta$  (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases associated with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

IT 438203-38-4P 438203-43-1P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as

protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

438203-38-4 CAPLUS RN

Acetamide, N-[4-[[4-(4-methoxyphenyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-CN 2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

438203-43-1 CAPLUS

4-Pyrimidinecarboxylic acid, 6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-[[4-[(1oxopropyl)amino]phenyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE 438203-35-1P 438203-36-2P 438203-41-9P

438203-45-3P 438203-48-6P 438205-29-9P

438205-30-2P 438205-31-3P 438205-32-4P

438205-34-6P 438205-36-8P 438205-38-0P

438205-40-4P 438205-41-5P 438205-42-6P

438205-43-7P 438205-44-8P 438205-46-0P

438205-47-1P 438205-48-2P 438205-49-3P

438205-50-6P 438205-51-7P 438205-52-8P

438205-53-9P 438205-54-0P 438205-55-1P

438205-56-2P 438205-57-3P 438205-58-4P

438205-59-5P 438205-60-8P 438205-61-9P

438205-62-0P 438205-63-1P 438205-64-2P

438205-65-3P 438205-66-4P 438205-67-5P 438205-68-6P 438205-69-7P 438205-70-0P

438205-71-1P 438205-72-2P 438205-73-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438203-35-1 CAPLUS

CN Acetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-36-2 CAPLUS

CN 4-Pyrimidinamine, 2-[[(4-methoxyphenyl)methyl]thio]-6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-41-9 CAPLUS

CN Acetamide, N-[4-[[4-[4-[3-(dimethylamino)propoxy]phenyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438203-45-3 CAPLUS

CN Propanamide, N-[4-[[4-(hydroxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

HO-
$$CH_2$$
NH- $C-Et$ 
Me

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-48-6 CAPLUS

CN Acetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-morpholinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-29-9 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-6-phenyl- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-30-2 CAPLUS

CN Benzoic acid, 3-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & \\ & & \\ &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

N 438205-31-3 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-(9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-32-4 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-5,6-dimethyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME).

RN 438205-34-6 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-5-methyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-36-8 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-methyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-38-0 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-40-4 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-(4-methyl-1-piperazinyl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

RN 438205-41-5 CAPLUS

CN 4-Pyrimidinamine, 6-(2,6-dimethylphenyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-42-6 CAPLUS

CN 4-Pyrimidinamine, 6-(2-methylphenyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

RN 438205-43-7 CAPLUS

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-6-phenyl- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-44-8 CAPLUS

CN Propanamide, 2-methyl-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-46-0 CAPLUS

CN Propanamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

RN 438205-47-1 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-48-2 CAPLUS

CN 1-Propanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-49-3 CAPLUS

CN Ethanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-50-6 CAPLUS

CN Acetamide, N-[4-[[4-(2-methylphenyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-51-7 CAPLUS

CN Butanamide, 3-methyl-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-52-8 CAPLUS

CN Acetamide, N-[4-[[5-methyl-4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-53-9 CAPLUS

CN Acetamide, N-[4-[[4-[3-(acetylamino)phenyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-54-0 CAPLUS

CN 2-Propanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-55-1 CAPLUS

CN Acetamide, 2-(dimethylamino)-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

RN 438205-56-2 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-57-3 CAPLUS

CN 4,6-Pyrimidinediamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(2-methoxyethyl)-N'-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

MeO-
$$CH_2$$
- $CH_2$ - $N$ 

N

S- $CH_2$ 

C1

Me

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-58-4 CAPLUS

CN 4-Pyrimidinamine, 6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-[(phenylmethyl)thio]- (9CI) (CA INDEX NAME)

RN 438205-59-5 CAPLUS

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-[(phenylmethyl)thio]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-60-8 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-61-9 CAPLUS

CN Acetamide, N-[4-[[4-(1,1-dimethylethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-62-0 CAPLUS

CN Propanamide, N-[4-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-63-1 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(1-piperidinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c} H \\ N \\ N \\ N \\ N \\ \end{array}$$
 
$$\begin{array}{c} N \\ S - CH_2 \\ \end{array}$$
 
$$\begin{array}{c} C1 \\ \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-64-2 CAPLUS

CN Morpholine, 4-[[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-morpholinyl)-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 438205-65-3 CAPLUS

CN Morpholine, 4-[[4-[[4-[(2-methoxyethyl)amino]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-66-4 CAPLUS

CN Morpholine, 4-[[4-[[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 438205-67-5 CAPLUS

CN Propanamide, N-[4-[[4-(methoxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-68-6 CAPLUS

CN Benzoic acid, 4-[[4-(methoxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & \\ & & \\ &$$

RN 438205-69-7 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3,5-dimethoxyphenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-70-0 CAPLUS.

CN 4-Pyrimidinamine, 2-[[(3,5-dimethoxyphenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(3-pyrrolidinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-71-1 CAPLUS

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-[(2-naphthalenylmethyl)thio]- (9CI) (CA INDEX NAME)

RN 438205-72-2 CAPLUS

CN Acetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-73-3 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-[[4-[(1-oxopropyl)amino]phenyl]thio]-, butyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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     2002:555487 CAPLUS
AN
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     Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase
ΤI
     inhibitors, especially of Aurora-2 and GSK-3
                                                            Same Same

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Prof.

20011219

Printing
     Bebbington, David; Charrier, Jean-Damien; Golec, Julian; Miller, Andrew;
IN
     Knegtel, Ronald
     Vertex Pharmaceuticals Incorporated, USA
PA
     PCT Int. Appl., 333 pp.
SO
     CODEN: PIXXD2
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OS MARPAT 137:125169

AB The title compds. I [Z1 = N, CR8; Z2 = N. CH; and at least one of Z1 and Z2 = N; Rb, Rc = TR3, LZR3; C2RbRc = (un)substituted fused (hetero)cycle; Q = NR4, O, S, etc.; R1 = TD; D = (un)substituted mono- or bicyclic(hetero)aryl, heterocyclyl, carbocyclyl; T = a bond, alkylidene (un)interrupted by O, S, NR4, CO, etc.; Z = alkylidene; L = O, S, SO, SO2, etc.; R2, R2a = R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, etc.; R = H, (un)substituted aliphatic, (hetero)aryl, heterocyclyl; R4 = R7, COR7, SO2R7, etc.; W = CO, CO2, CONR6, etc.; R6, R7 = H, alkyl; or N(R6)2 or N(R7)2 = heterocyclyl, heteroaryl] were prepared For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in tert-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20  $\mu M$ : GSK-3 $\beta$  (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases associated with protein kinases, such as diabetes, .cancer, and Alzheimer's disease (no data).

IT 438203-38-4P 438203-43-1P

> RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438203-38-4 CAPLUS

Acetamide, N-[4-[4-(4-methoxyphenyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-CN 2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438203-43-1 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-[[4-[(1-oxopropyl)amino]phenyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

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ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
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     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as
       protein kinase inhibitors for treatment of cancer, diabetes, and
       Alzheimer's disease)
RN
     438203-35-1 CAPLUS
CN
     Acetamide, N-[4-[(4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-
     pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)
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RN 438203-36-2 CAPLUS

CN 4-Pyrimidinamine, 2-[[(4-methoxyphenyl)methyl]thio]-6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-41-9 CAPLUS

CN Acetamide, N-[4-[[4-[4-[3-(dimethylamino)propoxy]phenyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438203-45-3 CAPLUS

CN Propanamide, N-[4-[[4-(hydroxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

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$$CH_2$$
NH- $C-Et$ 
Me

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-48-6 CAPLUS

CN Acetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-morpholinyl)-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-29-9 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-6-phenyl- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-30-2 CAPLUS

CN Benzoic acid, 3-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-31-3 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-(9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-32-4 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-5,6-dimethyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

RN 438205-34-6 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-5-methyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-36-8 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-methyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-38-0 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-40-4 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-(4-methyl-1-piperazinyl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

RN 438205-41-5 CAPLUS

CN 4-Pyrimidinamine, 6-(2,6-dimethylphenyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-42-6 CAPLUS

CN 4-Pyrimidinamine, 6-(2-methylphenyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

RN 438205-43-7 CAPLUS

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-6-phenyl- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-44-8 CAPLUS

CN Propanamide, 2-methyl-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} Ph & O \\ \parallel & NH-C-Pr-i \\ \hline \\ Me \end{array}$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-46-0 CAPLUS

CN Propanamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-47-1 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-48-2 CAPLUS

CN 1-Propanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-49-3 CAPLUS

CN Ethanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & & & & & & & & & & & \\ & & & & & & & & & & & & & \\ & & & & & & & & & & & \\ & & & & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & & \\ & & & & & & & & \\ & & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ &$$

RN 438205-50-6 CAPLUS

CN Acetamide, N-[4-[[4-(2-methylphenyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-51-7 CAPLUS

CN Butanamide,  $3-\text{methyl-N-[}4-[[4-[(5-\text{methyl-1H-pyrazol-3-yl)amino}]-6-\text{phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)$ 

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-52-8 CAPLUS

CN Acetamide, N-[4-[[5-methyl-4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-53-9 CAPLUS

CN Acetamide, N-[4-[[4-[3-(acetylamino)phenyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-54-0 CAPLUS

CN 2-Propanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-55-1 CAPLUS

CN Acetamide, 2-(dimethylamino)-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

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RN 438205-56-2 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-57-3 CAPLUS

CN 4,6-Pyrimidinediamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(2-methoxyethyl)-N'-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

MeO-
$$CH_2$$
- $CH_2$ - $N$ 

N
S- $CH_2$ 

C1

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-58-4 CAPLUS

CN 4-Pyrimidinamine, 6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-[(phenylmethyl)thio]- (9CI) (CA INDEX NAME)

RN 438205-59-5 CAPLUS

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-[(phenylmethyl)thio]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN .438205-60-8 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-61-9 CAPLUS

CN Acetamide, N-[4-[[4-(1,1-dimethylethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-62-0 CAPLUS

CN Propanamide, N-[4-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-63-1 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(1-piperidinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-64-2 CAPLUS

CN Morpholine, 4-[[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-morpholinyl)-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 438205-65-3 CAPLUS

CN Morpholine, 4-[[4-[[4-[(2-methoxyethyl)amino]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-66-4 CAPLUS

CN Morpholine, 4-[[4-[[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

 $438205-67-5 \quad \text{CAPLUS} \\ \text{Propanamide, N-[4-[[4-(methoxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-6-[(5-methyl-3-yl)amino]-6-[(5-methyl-3-yl)amino]-6-[(5-methyl-3-yl)amino]-6-[(5-methyl-3-yl)amino]-6-[(5-methyl-3-yl)amino]-6-[(5-methyl-3-yl)amino]-6-[(5-methyl-3-yl)amino]-6-[(5-methyl-3-yl)amino]-6-[(5-methyl-3-yl)amino]-6-[(5-methyl-3-yl)amino]-6-[(5-methyl-3-yl)amino]-6-[(5-methyl-3-yl)amino]-6-[(5-methyl-3-yl)amin$ CN 2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN438205-68-6 CAPLUS

CN Benzoic acid, 4-[[4-(methoxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2pyrimidinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

RN 438205-69-7 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3,5-dimethoxyphenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-70-0 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3,5-dimethoxyphenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(3-pyrrolidinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-71-1 CAPLUS

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-[(2-naphthalenylmethyl)thio]- (9CI) (CA INDEX NAME)

RN 438205-72-2 CAPLUS

CN Acetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-73-3 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-[[4-[(1-oxopropyl)amino]phenyl]thio]-, butyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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ANSWER 13 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
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     Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase
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     inhibitors, especially of Aurora-2 and GSK-3, for treatment of cancer,
     diabetes, and Alzheimer's disease
IN
     Bebbington, David; Charrier, Jean-Damien; Davies, Robert; Everitt, Simon;
     Kay, David; Knegtel, Ronald; Patel, Sanjay
                                                           Common Ins
     Vertex Pharmaceuticals Incorporated, USA
PA
     PCT Int. Appl., 342 pp.
SO
     CODEN: PIXXD2
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     English
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AB Title compds. I [wherein Z1 = N or CR8; Z2 = N or CH; and at least 1 of Z1 and Z2 = N; Rx and Ry = independently TR3 or LZR3; or C2RxRy = (un) substituted fused (hetero) cycle; Q = NR4, O, S, C(6a)2, 1,2-cyclo(prop/but)anediyl, or 1,3-cyclobutanediyl; R1 = TD; D = (un) substituted mono- or bicyclic (hetero) aryl, heterocyclyl, or carbocyclyl; T = a bond or alkylidene chain (un)interrupted by O, S, NR4, CO, CONH, NHCO, SO2, SO2NH, NHSO2, CO2, OCO, OCONH, or NHCO2, with provisos; Z = alkylidene chain; L = O, S, SO, SO2, NR6SO2, SO2NR6, NR6, NR6CO, NR6CO2, NR6CONR6, NR6SO2NR6, NR6NR6, OCONR6, or W; R2 and R2a = independently R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, COR, CO2R, CO(CH2)0-1COR, NO2, CN, SO0-2R, N(R4)2, carbamoyl, sulfamoyl, OCOR, acylamino, hydrazino, ureido, etc.; R = independently H or (un)substituted aliphatic, (hetero)aryl, or heterocyclyl; R4 = independently R7, COR7, carboxy, CON(R7)2, or SO2R7; W = CO, CO2,CONR6, C(R6)20, C(R6)2SO0-2, C(R6)2SO2NR6, C(R6)2NR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, or C(R6) 2NR6CONR6; R6, R6a, R7 = independently H or aliphatic; or N(R6) 2 or N(R7)2 = independently heterocyclyl or heteroaryl; or C(R6a)2 =carbocycle; R8 = R, halo, OR, COR, CO2R, COCOR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2(R4)2, OCOR, NR4COR, NR4CO2(aliphatic), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2] were prepared I are protein kinase inhibitors, especially of Aurora-2 and GSK-3. For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in t-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20  $\mu$ M: GSK-3 $\beta$  (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases associated with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

IT 438203-38-4P, [2-(4-Acetamidophenylsulfanyl)-6-(4methoxyphenyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine 438203-43-1P, [6-Methoxycarbonyl-2-(4propionylaminophenylsulfanyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3yl)amine

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438203-38-4 CAPLUS

CN Acetamide, N-[4-[[4-(4-methoxyphenyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-43-1 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-[[4-[(1-oxopropyl)amino]phenyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

438203-35-1P, [2-(4-Acetamidophenylsulfanyl)-6-phenylpyrimidin-4-yl] (5-methyl-1H-pyrazol-3-yl) amine 438203-36-2P,

[2-(4-Methoxybenzylsulfanyl)-6-(4-methylpiperazin-1-yl)pyrimidin-4-yl] (5-methyl-1H-pyrazol-3-yl) amine 438203-41-9P, [2-(4-Acetamidophenylsulfanyl)-6-[4-(3-dimethylaminopropoxy)phenyl]pyrimidin-4-yl] (5-methyl-1H-pyrazol-3-yl) amine 438203-45-3P,

[6-Hydroxymethyl-2-(4-propionylaminophenylsulfanyl)pyrimidin-4-yl] (5-methyl-1H-pyrazol-3-yl) amine 438203-48-6P, [2-(4-Acetamidophenylsulfanyl)-6-(morpholin-4-yl)pyrimidin-4-yl] (5-methyl-1H-pyrazol-3-yl) [2-(naphthalen-2-ylsulfanyl)-6-phenylpyrimidin-4-yl]amine 438205-30-2P, (5-Cyclopropyl-1H-pyrazol-3-yl) [2-(3-methoxycarbonylphenylsulfanyl)-6-phenylpyrimidin-4-yl]amine

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438205-31-3P, (5-Cyclopropyl-1H-pyrazol-3-yl)[2-(naphthalen-2-
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(5-Cyclopropyl-1H-pyrazol-3-yl)[5-methyl-2-(naphthalen-2-
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(5-Cyclopropyl-1H-pyrazol-3-yl)[6-methyl-2-(naphthalen-2-
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(5-Cyclopropyl-1H-pyrazol-3-yl)[6-(morpholin-4-yl)-2-(naphthalen-2-
ylsulfanyl)pyrimidin-4-yl]amine 438205-40-4P,
(5-Cyclopropyl-1H-pyrazol-3-yl)[6-(1-methylpiperazin-4-yl)-2-(naphthalen-2-
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[6-(2,6-Dimethylphenyl)-2-(naphthalen-2-ylsulfanyl)pyrimidin-4-yl](5-
methyl-1H-pyrazol-3-yl)amine 438205-42-6P, [6-(2-Methylphenyl)-2-
(naphthalen-2-ylsulfanyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine
438205-43-7P, (5-Methyl-1H-pyrazol-3-yl)[2-(naphthalen-2-
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438205-47-1P, [2-(4-Cyclopropylcarbonylaminophenylsulfanyl)-6-
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pyrazol-3-yl)amine 438205-50-6P, [2-(4-Acetamidophenylsulfanyl)-
6-(2-methylphenyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine
438205-51-7P, [2-(4-Isobutylcarbonylaminophenylsulfanyl)-6-
phenylpyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine 438205-52-8P
 [2-(4-Acetamidophenylsulfanyl)-5-methyl-6-phenylpyrimidin-4-yl](5-methyl-
1H-pyrazol-3-yl)amine 438205-53-9P, [6-(3-Acetamidophenyl)-2-(4-
acetamidophenylsulfanyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine
438205-54-0P, [2-(4-Isopropylsulfonylaminophenylsulfanyl)-6-
phenylpyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine 438205-55-1P
, [2-[[4-(2-Dimethylaminoacetylamino)phenyl]sulfanyl]-6-phenylpyrimidin-4-
yl] (5-methyl-1H-pyrazol-3-yl)amine 438205-56-2P
438205-57-3P 438205-58-4P, [2-Benzylsulfanyl-6-(4-
methylpiperazin-1-yl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine
438205-59-5P 438205-60-8P 438205-61-9P,
[2-(4-Acetamidophenylsulfanyl)-6-tert-butylpyrimidin-4-yl](5-methyl-1H-
pyrazol-3-yl)amine 438205-62-0P, (5-Cyclopropyl-1H-pyrazol-3-
yl) [6-phenyl-2-(4-propionylaminophenylsulfanyl)pyrimidin-4-yl]amine
438205-63-1P 438205-64-2P, (5-Methyl-1H-pyrazol-3-yl)[2-
[[4-(morpholinosulfonyl)benzyl]sulfanyl]-6-morpholin-4-ylpyrimidin-4-
yl]amine 438205-65-3P, [6-(2-Methoxyethylamino)-2-[[4-
(morpholinosulfonyl)benzyl]sulfanyl]pyrimidin-4-yl](5-methyl-1H-pyrazol-3-
yl)amine 438205-66-4P, [6-(4-Methylpiperazin-1-yl)-2-[[4-
(morpholinosulfonyl)benzyl]sulfanyl]pyrimidin-4-yl](5-methyl-1H-pyrazol-3-
yl)amine 438205-67-5P, [6-Methoxymethyl-2-(4-
propionylaminophenylsulfanyl)pyrimidin-4-yl]-(5-methyl-1H-pyrazol-3-
yl)amine 438205-68-6P, [2-(4-Methoxycarbonylphenylsulfanyl)-6-
methoxymethylpyrimidin-4-yl] (5-methyl-1H-pyrazol-3-yl)amine
438205-69-7P, [2-(3,5-Dimethoxybenzylsulfanyl)-6-morpholin-4-
ylpyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine 438205-70-0P,
[2-(3,5-Dimethoxybenzylsulfanyl)-6-pyrrolidin-4-ylpyrimidin-4-yl] (5-methyl-
1H-pyrazol-3-yl)amine 438205-71-1P, (5-Methyl-1H-pyrazol-3-yl)[6-
morpholin-4-yl-2-(naphthalene-2-ylmethylsulfanyl)pyrimidin-4-yl]amine
438205-72-2P, [2-(4-Acetamidophenylsulfanyl)pyrimidin-4-yl](5-
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methyl-1H-pyrazol-3-yl)amine 438205-73-3P,

[6-(1-Butoxycarbonyl)-2-(4-propionylaminophenylsulfanyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; preparation of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438203-35-1 CAPLUS

CN Acetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-36-2 CAPLUS

CN 4-Pyrimidinamine, 2-[[(4-methoxyphenyl)methyl]thio]-6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438203-41-9 CAPLUS

CN Acetamide, N-[4-[4-[4-[3-(dimethylamino)propoxy]phenyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN

438203-45-3 CAPLUS Propanamide, N-[4-[[4-(hydroxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-CN2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

HO-
$$CH_2$$
NH- $C-Et$ 
Me

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

438203-48-6 CAPLUS RN

CNAcetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-morpholinyl)-2pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-29-9 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-6-phenyl-(9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

· RN 438205-30-2 CAPLUS

CN Benzoic acid, 3-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ & & \\$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-31-3 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-(9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-32-4 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-5,6-dimethyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

RN 438205-34-6 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-5-methyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-36-8 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-methyl-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-38-0 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-40-4 CAPLUS

CN 4-Pyrimidinamine, N-(5-cyclopropyl-1H-pyrazol-3-yl)-6-(4-methyl-1-piperazinyl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

RN 438205-41-5 CAPLUS

CN 4-Pyrimidinamine, 6-(2,6-dimethylphenyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-42-6 CAPLUS

CN 4-Pyrimidinamine, 6-(2-methylphenyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)- (9CI) (CA INDEX NAME)

438205-43-7 CAPLUS

4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-2-(2-naphthalenylthio)-6-CN phenyl- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

438205-44-8 CAPLUS RN

Propanamide, 2-methyl-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-CN2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN

438205-46-0 CAPLUS
Propanamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME) CN

RN 438205-47-1 CAPLUS

CN Cyclopropanecarboxamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-48-2 CAPLUS

CN 1-Propanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-49-3 CAPLUS

CN Ethanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-50-6 CAPLUS

CN Acetamide, N-[4-[[4-(2-methylphenyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-51-7 CAPLUS

CN Butanamide, 3-methyl-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-52-8 CAPLUS

CN Acetamide, N-[4-[[5-methyl-4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-53-9 CAPLUS

CN Acetamide, N-[4-[[4-[3-(acetylamino)phenyl]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-54-0 CAPLUS

CN 2-Propanesulfonamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & & & & & \\ & & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & & \\ & & & & & \\ & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & \\ & & \\ &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-55-1 CAPLUS

CN Acetamide, 2-(dimethylamino)-N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-56-2 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-57-3 CAPLUS

CN 4,6-Pyrimidinediamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(2-methoxyethyl)-N'-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

MeO-
$$CH_2$$
- $CH_2$ - $N$ 

N

S- $CH_2$ 

Me

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-58-4 CAPLUS

CN 4-Pyrimidinamine, 6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)-2-[(phenylmethyl)thio]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE RN 438205-59-5 CAPLUS

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-[(phenylmethyl)thio]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-60-8 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-6-(4-methyl-1-piperazinyl)-N-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-61-9 CAPLUS

CN Acetamide, N-[4-[[4-(1,1-dimethylethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

RN 438205-62-0 CAPLUS

CN Propanamide, N-[4-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-6-phenyl-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-63-1 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3-chlorophenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(1-piperidinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-64-2 CAPLUS

CN Morpholine, 4-[[4-[[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-6-(4-morpholinyl)-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 438205-65-3 CAPLUS

CN Morpholine, 4-[[4-[[4-[(2-methoxyethyl)amino]-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-66-4 CAPLUS

CN Morpholine, 4-[[4-[[[4-(4-methyl-1-piperazinyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]methyl]phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

RN 438205-67-5 CAPLUS

CN Propanamide, N-[4-[[4-(methoxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$$

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-68-6 CAPLUS

CN Benzoic acid, 4-[[4-(methoxymethyl)-6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

RN 438205-69-7 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3,5-dimethoxyphenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-70-0 CAPLUS

CN 4-Pyrimidinamine, 2-[[(3,5-dimethoxyphenyl)methyl]thio]-N-(5-methyl-1H-pyrazol-3-yl)-6-(3-pyrrolidinyl)- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-71-1 CAPLUS

CN 4-Pyrimidinamine, N-(5-methyl-1H-pyrazol-3-yl)-6-(4-morpholinyl)-2-[(2-naphthalenylmethyl)thio]- (9CI) (CA INDEX NAME)

RN 438205-72-2 CAPLUS

CN Acetamide, N-[4-[[4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]thio]phenyl]- (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

RN 438205-73-3 CAPLUS

CN 4-Pyrimidinecarboxylic acid, 6-[(5-methyl-1H-pyrazol-3-yl)amino]-2-[[4-[(1-oxopropyl)amino]phenyl]thio]-, butyl ester (9CI) (CA INDEX NAME)

ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

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(FILE 'HOME' ENTERED AT 09:17:43 ON 25 OCT 2006)

FILE 'REGISTRY' ENTERED AT 09:17:54 ON 25 OCT 2006

L1 STRUCTURE UPLOADED

L2 10 S L1 SSS SAM

L3 179 S L1 SSS FUL

FILE 'CAPLUS' ENTERED AT 09:19:35 ON 25 OCT 2006

L4 13 S L3

FILE 'CAOLD' ENTERED AT 09:20:28 ON 25 OCT 2006

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L5 0 L3

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COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 0.44 235.36

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL

ENTRY SESSION

CA SUBSCRIBER PRICE 0.00 -9.75

STN INTERNATIONAL LOGOFF AT 09:20:39 ON 25 OCT 2006

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Application Number	Submit	
IDS Flag Clearance for	Application 10632428	



Content	Mailroom Date	Entry Number	IDS Review	Last Modified	Reviewer
M844	2006-08-03	29	Y	2006-10-25 14:04:11.0	DRao
M844	2003-08-01	11	Y 🔽	2006-02-02 10:29:09.0	jjohnsen1
Update			,		